REMARKS

Claims 5-27, 31-50, 53 and 54 are pending. Claims 5-27, 31 and 32 have been withdrawn from consideration. Claims 5-27, 31, 32, 39, 50 and 54 are cancelled herein without prejudice. Claims 33, 36, 37, 40 and 41 have been amended. Support for the amendments can be found throughout the application as filed. Specifically, support for the amendment to claim 33 can be found, for example, in former claim 39. Claims 36, 37, 40 and 41 have been amended to provide proper antecedent basis. Accordingly, the amendments do not raise an issue of new matter and entry thereof is respectfully requested. Following entry of the amendments, claims 33-38, 40-49 and 53 will be under examination in the above-identified application.

Rejections Under 35 U.S.C. § 112

Claims 39-41 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking written description. In this regard, the Office asserts that the description in the specification of the genus histones fails to represent the genus of histone analog. The Office further asserts that the specification fails to define histones analogues or provide an exemplary structure of a histone analog to show that applicant was in possession of the claimed method at the time the application was filed. Applicants respectfully traverse this ground of rejection for the reasons that follow.

Applicant respectfully directs the Examiner's attention to the recent Federal Circuit decisions that have further clarified the written description requirement. In the recent decision of *Moba v. Diamond Automation*, 325 F.3d 1306, 66 USPQ2d 1429 (Fed.Cir. 2003) the Federal Circuit stated:

> [C]ase law reflects two applications of [the written description requirement,] . . . "[t]he function of the description requirement is to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him. . . . In that setting, the written description is the metric against which a subsequently added claim is measured to determine if it is due the priority date of the original patent. . . . The second application of the written description requirement is reflected in Regents of the *University of*

> *California v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997). There, this court invoked the written description requirement in a case without priority issues, [requiring a] precise definition of a DNA sequence in the patent specification. **In more recent cases, however, this court has distinguished *Lilly*. . . . The *Lilly* disclosure rule does not require a particular form of disclosure** because one of skill could determine from the specification that the inventor possessed the invention at the time of filing.

Id. at 1319 (Emphasis added).

Similarly, in *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002), after initially holding that a reference to specified biological material in a public depository was not a sufficient written description, the court on rehearing indicated that *Lilly* did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement and held the written description requirement may be satisfied if, in the knowledge of the art, the disclosed function is sufficiently correlated to a particular, known structure.

In its first pronouncement following *Enzo*, the Federal Circuit again followed this rationale in *Amgen Inc. v. Hoechst Marion Roussel Inc.*, 314 F.3d 1313, 1332, 65 USPQ2d 1385, 1399 (Fed. Cir. 2003). The Federal Circuit recently extended this rationale to binding polypeptides such as antibodies in *Noelle v. Lederman*, Case No. 02-1187 (Fed. Cir., Jan. 20, 2004). The Court in *Noelle* stated that written description for antibodies relying on functional characteristics can be met if function is coupled with a disclosed correlation to a known structure.

Claim 33, as amended, is directed to a method to identify an agent that increases or decreases the amount of double minute chromosomes or extrachromosomal DNA in a cell. The method consists of contacting a cell expressing a labeled histone or analog thereof with an agent. The application provides adequate written description of histone analogs at least because the application describes that histone analogs can be used in the claimed methods and because, similar to histones, particular structures of histone analogues are well known in the art.

For example, histones have been the subject matter of many studies over the years and can be found described in many molecular or cell biology text books. Exemplary publications supporting the particular knowledge in the art of histones and their structure were cited in Applicants' previous response (see, for example, previous Exhibits A and B to Meyers, R.A., *Molecular Biology and Biotechnology, A Comprehensive Desk Reference*, VCH Publishers, Inc., 413-17, (1995), and Lodish, H. et al., *Molecular Cell Biology*, Scientific American Books, 3rd Ed., 315-16, 346-348, (1995)). Further, the application describes, for example, at pages 44-50 the use of variously labeled histones that can associate with double minute chromosomes or extrachromosomal DNA and form a labeled complex.

Similarly, amino acid and polypeptide analogs also are well known in the art. For example, particularly known structures of amino acid analogs include modified forms of naturally and non-naturally occurring amino acids. Naturally occurring amino acids include the 20 (L)-amino acids utilized during protein biosynthesis as well as others such as 4-hydroxyproline, hydroxylysine, desmosine, isodesmosine, homocysteine, citrulline and ornithine, for example. Non-naturally occurring amino acids include, for example, (D)-amino acids, norleucine, norvaline, p-fluorophenylalanine, ethionine and the like.

Applicants previously submitted evidence for the above and other well known structures of amino acid analogs that are included within the description of histone analogs. For example, particularly known structures of amino acid analogs can be found described in, for example, Roberts and Vellaccio, *The Peptides: Analysis, Synthesis, Biology*, Eds. Gross and Meinhofer, Vol. 5, pp. 341-358, Academic Press, Inc., New York, New York (1983), submitted previously as Exhibit C. Other examples include peralkylated amino acids, particularly permethylated amino acids, which can be found described in, for example, *Combinatorial Chemistry*, Eds. Wilson and Czarnik, Ch. 11, pp. 235-237, John Wiley & Sons Inc., New York, New York (1997), previous Exhibit D. Yet other examples include amino acids whose amide portion (and, therefore, the amide backbone of the resulting peptide) has been replaced, for example, by a sugar ring, steroid, benzodiazepine or carbo cycle. An exemplarly description of these analogs can be found described in, for example, *Burger's Medicinal Chemistry and Drug*

Discovery, Ed. Manfred E. Wolff, Ch. 15, pp. 619-627, John Wiley & Sons Inc., New York, New York (1995), previous Exhibit E.

Further, the application provides descriptions of well known histone polypeptides and cites to publications in the art describing such histone polypeptides and their properties. The application additionally describes specific histones having a correlation with a particular, known structure. As described previously, the histones and histone analogs of the invention have well known properties that correlate with chromosomal binding. Accordingly, such histones, histone analogs, their structures and activities are well known in the art. Because histones and histone analogs, their structures and activities are well known in the art, the application adequately describes the claimed histone analogs that associate with double minute chromosomes or extrachromosomal DNA to form a labeled complex.

In light of the above remarks, Applicants maintain that the application provides adequate written description of the claimed invention to satisfy the first paragraph of § 112. Accordingly, this ground of rejection is respectfully requested to be withdrawn.

Rejections Under 35 U.S.C. § 103

Claims 33-38, 42-50, 53 and 54 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Robinett et al. in view Abken et al. Robinett et al. is stated to describe a method for visualizing chromosomes. Abken et al. is stated to describe extrachromosomal DNA and double minute DNA to be chromosomal in origin and that double minute DNA can be eliminated from cancer cells in response to drug administration. Abken et al. is further asserted to describe that agents that reduce double minute DNA formation can be a basis for therapeutic strategis.. The Office Action alleges that it would have been obvious to use the visualization method described by Robinett et al. in a method for identifying agents that decrease or increase double minute chromosome formation because Robinett et al. provides a method for determining changes in extrachromosomal DNA. Applicants respectfully traverse this ground of rejection for the reasons that follow.

Applicants contend that the claimed method to identify an agent that increases or decreases the amount of double minute chromosomes or extrachromosomal DNA in a cell is unobvious over Robinett et al. and Abken et al. However, to further prosecution of this application, claim 33 has been amended to recite that the claimed agent used in the method of identifying a agent that alters the amount of extrachromosomal DNA is a histone or analog thereof. This element can be found in claim 39, which has been cancelled above. Accordingly, claim 33 now recites all the elements of former claim 39, which stands unobvious over the citations to Robinett et al. and Abken et al. Accordingly, this ground of rejection is moot and Applicant respectfully requests its withdrawal.

CONCLUSION

In light of the Amendments and Remarks herein, Applicants submit that the claims are in condition for allowance and respectfully request a notice to this effect. Should the Examiner have any questions, she is invited to call the undersigned attorney.

Respectfully submitted,

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